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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/442,111	11/17/1999	SHAWN DEFREES	14137-013820	5434

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EXAMINER

FRONDA, CHRISTIAN L

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 02/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/442,111

Applicant(s)

DEFREES ET AL.

Examiner

Christian L Fronda

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 53 and 55-72 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 53 and 55-72 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 November 1999 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>14 and 17</u> . | 6) <input type="checkbox"/> Other: ____. |

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DETAILED ACTION

1. In the amendment dated 2/19/2002 (Paper No. 13), Applicants have amended claims 53 and 59, canceled claim 54, and added new claim 72.
2. Claims 53 and 55-72 are under consideration in this Office Action. New rejections and new grounds of rejection are presented in the instant Office Action.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
4. Claims 53 and 55-72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are genus claims which encompass any method for producing any oligosaccharide or glycolipid of any structure and composition by contacting any acceptor saccharide with any microorganism or any plant cell comprising any "accessory enzyme for forming a nucleotide sugar" and any heterologous glycosyltransferase. The scope of the claims that includes many oligosaccharides, glycolipids, glycosyltransferases, acceptor saccharides, and glycosyltransferase fusion proteins with widely differing structural, chemical, and physical characteristics and other oligosaccharides, glycolipids, glycosyltransferases, acceptor saccharides and glycosyltransferase fusion proteins which have yet to be discovered. Furthermore, the genus is highly variable because a significant number of structural differences between genus members is permitted.

The specification only provides a written description of one representative member of the claims genus, specifically, a transformed *E. coli* expressing a CMP-sialic acid synthetase/alpha 2,3-sialyltransferase fusion protein is used in the production of 3'-sialyllactose. However, the specification does not disclose the specific amino acid sequence of the fusion protein. Furthermore, the specification fails to provide a written description of additional representative oligosaccharides, glycolipids, glycosyltransferases, and glycosyltransferase fusion proteins as

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encompassed by the genus claims. Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Amending the claims to recite the specific amino acid sequence and identity of the fusion protein may overcome this rejection.

5. Claim 53 and 55-72 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claims encompass any method for producing any oligosaccharide or glycolipid of any structure and composition by contacting any acceptor saccharide with any microorganism or any plant cell comprising any "accessory enzyme for forming a nucleotide sugar" and any heterologous glycosyltransferase.

The specification provides guidance for a transformed *E. coli* expressing a CMP-sialic acid synthetase/alpha 2,3-sialyltransferase fusion protein is used in the production of 3'-sialyllactose. However, the specification does not disclose the specific amino acid sequence of the fusion protein.

The standard for meeting the enablement requirement is whether one of skill in the art can make the invention without undue experimentation. The amount of experimentation to make the claimed invention is undue and outside the scope of routine experimentation since one must search for and screen for any oligosaccharide or glycolipid of any structure and composition to make, search for and screen for any glycosyltransferases of any sequence/structure and biological source which can be made into a bifunctional fusion protein, search for and screen for any acceptor saccharides, transform any microorganism or plant cell with a polynucleotide construct encoding the bifunctional fusion protein, and determining whether the transformant can produce the desired oligosaccharide or glycolipid. Teachings regarding how to search for and screen for the desired glycosyltransferase fusion protein is not guidance on how to make the fusion protein. Furthermore, predicting whether any glycosyltransferase fusion protein is successful in making any desired oligosaccharide or glycolipid is extremely low since no information is provide by the specification regarding the specific identity and sequence/structure of any other

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glycosyltransferase fusion protein.

Amending the claims to recite the specific amino acid sequence and identity of the fusion protein may overcome this rejection.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 53 and 55-72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is vague and indefinite because it is not clear how an oligosaccharide or glycolipid product can be produced with the recited steps of contacting the acceptor saccharide with the recited microorganism or plant cell. Clarification is required where the method includes steps for permeabilizing the cell, adding sugar substrates, allowing the reaction to take place, and detecting/determining the presence of the produced oligosaccharide (see Example 1, A-C, in the specification).

Claim 55 lacks antecedent basis and does not further limit the invention since claim 53 requires a heterologous glycosyltransferase but claim 55 now requires the glycosyltransferase to be endogenous.

Claim Rejections - 35 U.S.C. § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 53, 56, 57, 58, and 72 are rejected under 35 U.S.C. 102(b) as being anticipated by Samain et al. (Carbohydr Res. 1997 Jul 11;302(1-2):35-42) [reference cited in the IDS filed

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3/24/2003].

Samain et al. teach a method for making penta-N-acetyl-chitopentaose (2.5g/L) by culturing a *E.coli* transformed with heterologous genes, specifically, expressing *nodC* or *nodBC* genes (see Abstract and entire publication). Samain et al teach that UDP-N-acetylglucosamine is the sugar donor for synthesis of N-acetylated chitooligosaccharide by NodC (see "(4)", left column, p. 36). The taught NodC (chitin oligosaccharide synthase E.C. 2.4.1.16) "consists essentially" of a catalytic domain of a glycosyltransferase. Samain et al teach that the said *E.coli* cells were cultured and disrupted by boiling and the produced chitooligosaccharides were purified by charcoal adsorption and ion-exchange chromatography.

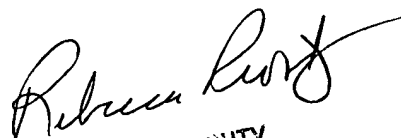
In absence of facts to the contrary the said *E.coli* inherently has an "accessory enzyme" for forming a nucleotide sugar", specifically, N-acetylglucosamine-1-phosphate uridylyltransferase encoded by the *glmU* gene which is required for making UDP-N-acetylglucosamine (see enclosed reference Mengin-Lecreux et al. J Bacteriol. 1994 Sep;176(18):5788-95).

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L. Fronda whose telephone number is (571)272-0929. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571)272-0928. The official fax phone number (703)872-9306. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (571)272-1600.

CLF


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PRIMARY EXAMINER
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